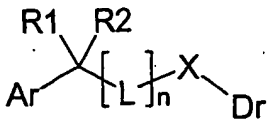
CLAIMS

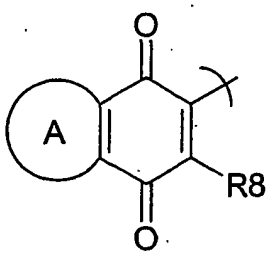
1. A compound of formula (1), or a pharmaceutically acceptable salt thereof,



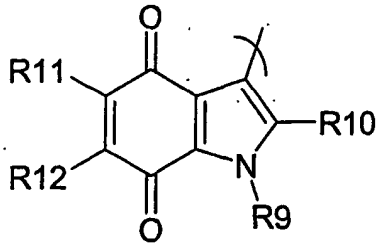
(1)

wherein:

- Ar is a substituted aryl or heteroaryl group bearing at least one nitro or azido group or is a group of formula (2) or (3)



(2)



(3)

- R_1 and R_2, which may be the same or different are independently optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, aryl, COR_3 or, together with the intervening carbon atom, form an optionally substituted heterocycloalkyl or carbocyclic ring ;
- L is -OC(O)- or -OP(O)(OR_6)-;
- n is 0 or 1;
- X is O, S, NR_7 or a single covalent bond;
- R_3 is OR_4 or NR_4R_5;
- R_4, R_5, R_6 and R_7 are each independently hydrogen or optionally substituted alkyl or,

  where R_3 is NR_4R_5, R_4 and R_5 can be joined to form, together with the intervening nitrogen atom, a heterocycloalkyl ring;
- R_8 is hydrogen, alkoxy or dialkylaminoalkyl;

- R_9 is optionally substituted alkyl;
- R_{10} is hydrogen, alkyl, alkoxy or dialkylaminoalkyl;
- R_{11} and R_{12} are independently hydrogen, alkyl, alkoxy, thioalkoxy, amino, alkylamino, dialkylamino, morpholino, piperidino,piperazino or 1-aziridinyl;
- A is an optionally substituted aryl or heteroaryl ring; and
- Dr is a moiety such that DrXH represents a cytotoxic or cytostatic compound.

2. A compound according to claim 1, wherein the alkyl, alkenyl and alkynyl groups in the R_1 to R_{12} substituents are unsubstituted or substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, amino, mono(C_1-C_4 alkyl)amino, di(C_1-C_4 alkyl)amino, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio and (C_1-C_4 alkyl)sulphonyl groups.

3. A compound according to any one of the previous claims, wherein aryl and heteroaryl groups in the Ar, A and R_1, R_2 substituents are unsubstituted or substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C_1-C_6 alkyl, hydroxy, amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy.

4. A compound according to any one of the previous claims, wherein the heterocycloalkyl ring and carbocyclic rings in the R_1 to R_3 substituents are unsubstituted or substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C_1-C_6 alkyl, hydroxy, amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy.

5. A compound according to any one of the previous claims, wherein R_1 and R_2, together with the carbon to which they are attached, form a 3 to 10 membered heterocycloalkyl ring or a C_{3-10} carbocyclic ring, which ring is unsubstituted or substituted by 1, 2 or 3 unsubstituted substituents selected from halogen, C_1-C_6 alkyl, hydroxy, amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy.

6. A compound according to claim 5, wherein R_1 and R_2, together with the carbon to which they are attached, form a 5 to 6 membered heterocycloalkyl ring, which ring is unsubstituted or substituted by one unsubstituted C_1-C_2 alkyl group.

7. A compound according to any one of claims 1 to 4, wherein R_1 and R_2 are the same or different and each represent unsubstituted C_1-C_6 alkyl, unsubstituted C_1-C_6 alkenyl, unsubstituted C_1-C_6 alkynyl, a COR_3 group, an unsubstituted phenyl group or a phenyl group which is substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C_1-C_6 alkyl, hydroxy, amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy.

8. A compound according to claim 7, wherein R_1 and R_2 are the same or different and each represent unsubstituted C_1-C_4 alkyl, unsubstituted C_1-C_4 alkenyl, unsubstituted C_1-C_4 alkynyl, a COR_3 group, an unsubstituted phenyl group or a phenyl group which is substituted with 1, 2 or 3 unsubstituted substituents selected from halogen, C_1-C_4 alkyl, hydroxy, amino, C_1-C_2 haloalkyl, C_1-C_2 alkoxy and C_1-C_2 haloalkoxy.

9. A compound according to claim 7 or 8, wherein R_3 is hydroxy, unsubstituted C_1-C_4 alkoxy or NR_4R_5, wherein R_4 and R_5 are the same or different and each represent hydroxy or unsubstituted C_1-C_4 alkoxy, or R_4 and R_5 form, together with the nitrogen atom to which they are attached, a 3 to 10 membered heterocycloalkyl ring, which ring is unsubstituted or substituted by 1, 2 or 3 unsubstituted substituents selected from halogen, C_1-C_6 alkyl, hydroxy, amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy.

10. A compound according to claim 9, wherein R_3 is hydroxy, unsubstituted C_1-C_2 alkoxy or NR_4R_5, wherein R_4 and R_5 are the same or different and each represent hydrogen or unsubstituted C_1-C_4 alkyl.

11. A compound according to any one of claims 7 to 10, wherein R_1 and R_2 are the same or different and each represent unsubstituted C_1-C_2 alkyl or an unsubstituted -CO_2-(C_1-C_2 alkyl) group.

12. A compound according to any one of the preceding claims wherein n is 0 and X is O or S.

13. A compound according to any one of claims 1 to 11, wherein n is 1 and X is NH.

14. A compound according to any one of claims 1 to 11 or 13, wherein n is 1 and L is -OC(O)- or -OP(O)(OR6), wherein R_6 is hydrogen or unsubstituted C_{1-6} alkyl.

15. A compound according to claim 14, wherein L is -OC(O)-.

16. A compound according to any one of the previous claims, wherein Ar is a substituted aryl or heteroaryl group, which group carries one substituent selected from nitro and azido substituents and 0, 1 or 2 further unsubstituted substituents chosen from halogen, C_1-C_6 alkyl, hydroxy, amino, C_1-C_4 haloalkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkoxy substituents .

17. A compound according to claim 16, wherein Ar is a phenyl group or a 5-or 6-membered heteroaryl group, which group carries only one substituent which substituent is selected from nitro and azido substituents.

18. A compound according to claim 17, wherein Ar is an unsubstituted group selected from nitrophenyl, nitroimidazole, nitrothiophene and nitrofuranyl groups.

19. A compound according to any one of the previous claims, wherein DrXH is selected from an anthracyclin antibiotic, an antimetabolite, a topoisomerase inhibitor, an inhibitor of mitosis, inhibitors of protein kinases and an antagonist of (6*R*)-5,6,7,8-tetrahydrobiopterin.

20. A compound according to claim 19, wherein DrXH is selected from doxorubicin, epirubicin, daunorubicin, 5-fluorouracil, 6- mercaptopurine, 6-thioguanine, cytarabine, gemcitabine, capecitabine, fludarabine, cladribine, decitabine (5-aza-2'-deoxycytidine), troxacitabine (2'-deoxy-3'-oxacytidine), 5-azacytidine, 4'-thioaracytidine, tezacitabine, clofarabine, trimetrexate and methotrexate, etoposide and teniposide, topotecan, SN38, combretastatin A4, combretastatin A1, podophyllotoxin, vinblastine, vincristine vinorelbine, paclitaxel and docetaxel, an epothilone, deoxyepothilone B BMS 247550, a dolastatin derivative, a cryptophycin derivative, gefitinib, erlotinib, ZD6474 and AZD2171.

21. A compound according to claim 20, wherein DrXH is combretastatin A4, etoposide, cytarabine or 6-mercaptopurine.

22. A compound according to any one of the previous claims which is 1-(4-Methoxy-3-(2-(5-nitrothiophen-2-yl)propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-*Z*-ethene,1-(4-Methoxy-3-(2-(4-nitrophenyl)propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-*Z*-ethene,9-(7,8-Dihydroxy-2-methyl-hexahydro-pyrano[3,2-d][1,3]-dioxin-6-yloxy)-5-{3,5-dimethoxy-4-[1-methyl-1-(4-nitrophenyl)-ethoxy]-phenyl}-5,8,8a,9-tetrahydro-5aH-furo[3',4':6,7]naphtho[2,3-d][1,3]dioxol-6-one, 6-(2-(4-nitrophenyl)propan-2-ylsulfanyl)-9H-purine, 1-(4-Methoxy-3-(1-methyl-4-(5-nitrothien-2-yl)piperidin-4-yl)oxycarbonyloxy)phenyl-2-(3,4,5-trimethoxy)phenyl-*Z*-ethene, 1-(4-Methoxy-3-(2-(1-methyl-2-nitroimidazol-5-yl)propan-2-yl)oxyphenyl-2-(3,4,5-trimethoxy)phenyl-*Z*-ethene, 6-(2-(5-nitrothien-2-yl)propan-2-ylsulfanyl)-9H-purine, N^4-(2-(5-nitrothien-2-yl)prop-2-yl)oxycarbonyl-1-β-D-arabinofuranosylcytosine, 1-(3-(1-Ethoxycarbonyl-1-(5-nitrothien-2-yl)ethoxy)-4-methoxy-phenyl)-2-(3,4,5-trimethoxyphenyl)-*Z*-ethene and N-(2-{3-[1-Methyl-1-(5-nitro-thiophen-2-yl)-ethoxy]-phenyl}-ethyl)-acetamide, or a pharmaceutically acceptable salt thereof.

23. A pharmaceutical composition comprising a compound according to any one of the previous claims, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier or diluent.

24. A compound according to any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, for use in the treatment of the human or animal body.

25. Use of a compound as defined according to any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the prevention or treatment of a proliferative disorder.

26. Use according to claim 25, wherein the proliferative disorder is cancer, rheumatoid arthritis, psoriatic lesions, diabetic retinopathy or wet age-related macular degeneration.

27. Use according to claim 25 or 26, wherein the proliferative disorder is a hypoxic disorder.

28. Use according to any one of claims 25 to 28, wherein the medicament is for use in the prevention or treatment of a solid tumour or leukaemia.

29. A method of ameliorating or reducing the incidence of a proliferative disorder as defined according to any one of claims 25 to 28 in a patient, which method comprises administering to said patient an effective amount of a compound as defined in any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof.

30. A method according to claim 29, which method comprises administering to said patient an effective amount of

(a) a compound as defined in any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof; and

(b) a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene.

31. A product containing

(a) a compound as defined in any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof; and

(b) a reductase, an anti-body reductase conjugate, a macromolecule-reductase conjugate or DNA encoding a reductase gene for the simulataneous, separate or sequential use in the treatment of a proliferative disorder as defined in any one of claims 25 to 28.